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Ebola Virus and Its Immunopathogenesis - A Review

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Abstract

Ebola virus, a highly pathogenic DNA virus, is associated with severe systemic complications in both man and animals. Ebola virus is transmitted through direct and indirect contact. The first Ebola virus outbreak was due to the zoonotic transmission followed by human to human. These viruses encompass serious pathophysiological events like systemic viral replication, immune suppression, abnormal inflammatory responses, major fluid and electrolyte losses and high mortality. Diagnosis and laboratory tests, typically real time reverse transcription PCR is used to detect viral genome. The 2013 - 2016 outbreak was classified by WHO as a public health emergency of international concern, which drew attention to the challenges of diseases caused by infection with Ebola virus and societal preparation to handle future epidemics. This review throws insight on the immune-pathogenesis of ebola viruses from the articles retrieved from various search engines like Pubmed and Google scholar.

Keywords*: Ebola virus, Immuno-pathogenesis, Viral marker, Genome detection, Markers*

Introduction

Ebola virus disease was formerly known as ebola hemorrhagic disease. In Guinea during December 2013 the first case of ebola virus was reported. Ebola virus was found to be one among Filoviruses' family. Ebola virus disease is caused by many clades viz., BDBV, EBOV, SUDV or TAFV[1]. Until 2013, most Ebola virus outbreaks originated from middle Africa [2]. Ebola virus is a dangerous form of virus which has no treatment. Although the first case of human infection was probably acquired from an animal, all subsequent cases are likely to have arisen from human-to- human transmission [3]. The duration of epidemic growth in each region of each country, and the number of people at risk, were determined in part by the timing and magnitude of the interventions against Ebola. After the epidemic peak in each country, the case incidence declined most quickly in Liberia and more slowly in Sierra Leone and Guinea [4].

None of the health care workers reported to be infected globally and had died from ebola virus disease. So, it appears that aggressive supportive care can reduce mortality. However, there is no definite treatment for this virus, so it will lead to mortality [90%] [5]. Ebola virus is one of the most deadly pathogens known to infect humans and the origin of infection was a carrier who survived EVD in November 2014 [2,7]. In this outbreak, which generated 13 confirmed and probable cases, infection spread from Nzerekore to Macenta prefecture in Guinea and into Mon- rovia [8]. The persistent risk of infection from survivors is another reason (in addition to locally high rates of transmission) why we can expect any large Ebola epidemic to have a protracted end, demanding heightened surveillance, with routine testing of live and dead persons in whom EVD is suspected, for months after an outbreak ended [9]. This review thus highlights an overview on ebola virus and its immuno-pathogenesis.

Ebola Virus: An Overview:

The literature of the review was retrieved from search engines such as Pubmed, MESH, Google scholar and from other online sources**.** All the articles relevant to the topic of the review were included. The articles with general information were excluded from the study. The review was purely based on the previous reports published by other esteemed authors.

EBOLA VIRUS STRUCTURE AND GENOME:

Ebola virus is a RNA virus with the length of the viral particle around 300~1500 nm. It occurs primarily on the African continent. Strains from Zaire, Sudan, Tai Forest, and Bundibugyo with Zaire Ebola virus are considered as the lethal strain [10,11]. Researchers have found a fifth strain termed Reston in the Philippines. The strain infects primates, pigs, and humans and causes few if any symptoms and no deaths in humans. Ebola virus consists of 5 viral species within the genus ebolavirus [12]. It was found that people with Ebola virus had sudden onset of fever and malaise, accompanied by other nonspecific signs such as myalgia, headache, vomiting and diarrhea [10]. Among EVD patients 30% - 50% experienced hemorrhagic symptoms [13]. The outbreak was more during 1967, that time people were affected with EVD massively. 20 EVD outbreaks across central africa, species like Zaire ebolavirus, historically proven high case fatality upto 90% [14].

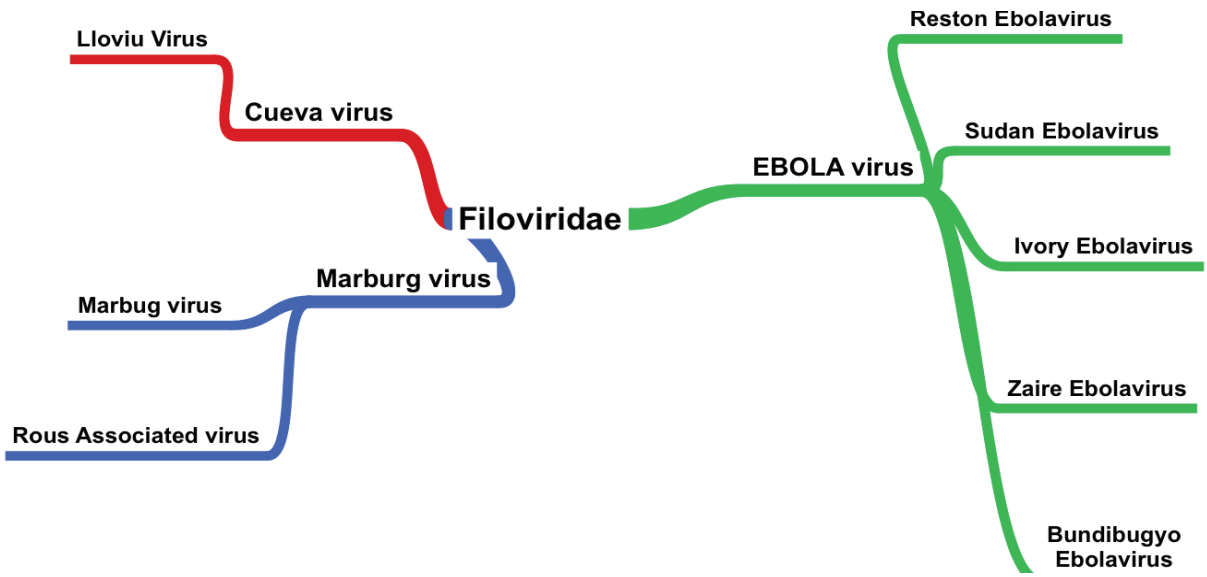

Figure 1: Taxonomy and clades of EBOLA virus

CLINICAL MANIFESTATIONS:

Ebola virus is most commonly transmitted when secretion from an infected patient comes in contact with mucosa or conjunctiva. Ebola virus replication requires attachment to a cell's membrane, binding to specific cell receptors and fusion with the cell's membrane. The virions glycoprotein [15,16], the outer capsule, is responsible for the attachments of the virus to the cell [17,18]. Ebola virus does not fuse to the cell membrane[19]. Death occurs as a result of circulatory shock or more commonly, multisystem organ dysfunction [20]. Nucleosome remodelers have been identified which causes repression of viral infection during the early stages [21]. Viral hemorrhagic disease, caused by members of the flaviviridae, Bunyavidae, viral families are characterised by fever, bleeding diathesis followed by circulatory collapse and death [22]. Filaviviridae family viruses are responsible for yellow fever and dengue fever [23].

IMMUNE RESPONSES

The patients who have poor immune response and high inflammatory response are mostly affected with Ebola virus disease. Host innate immune responses are vital in restricting the spread of viral infections including that of Ebola virus [24]. Antibodies could also function by recruiting cells and proteins of the immune system to destroy and clear the pathogen and its infected cells [25]. In most of the cases, both humoral and cellular immune response plays a vital role [26]. Cellular immune response involves the role of the natural killer cells and other immune cells[27]. The proinflammatory cytokines do play their role in viral evasion and protection. Both neutralizing and cross-reacting antibodies help in viral

clearance in the infected individuals [24].

DIAGNOSTIC METHODS TO DETECT THE ANTIGENS

Laboratory diagnosis of Ebola is achieved in two ways: detection of infectious particles (or particle components) in affected individuals and measurement of specific immune responses to Ebola virus**.** The incubation period of ebola virus disease is from 2 to 21 days, with shorter incubation periods correlating with exposure to a larger viral load. Viremia correlates with the abrupt onset of symptoms and signs of the disease [28]. According to WHO's protocol, it is like the sudden onset of high fever and headache, vomiting, diarrhoea, stomach pain, dyspnea, hiccuping [29,27]. Conventional diagnostic methods were replaced with RT-PCR tests for Ebola virus, developed by the CDC, and was first evaluated on serum samples collected from acutely ill patients [30]. Serological diagnostic methods to detect both IgG and IgM antibodies are also employed in certain conditions[31].

TREATMENT STRATEGIES

Although vaccination probably helped to reduce the rate of transmission after April 2015, the dominant interventions used have been the classic methods of Ebola control. Finding symptomatic cases and tracing potentially infected contacts, isolating cases, admitting patients to specially designed Ebola treatment centers, and providing supportive clinical care; and ensuring safe and dignified burial are also in the guidelines in the ebola viral disease prevention [32]. With no proper treatment strategies until now, increase in mortality rate is by immuno-pathogenic mechanisms that leads to develop shock and DIC [33]. It is capable of causing death in humans and non humans within a few days of exposure [34]. The epidemics that have occurred during the past 4 decades have been in low income countries with limited healthcare resources [35]. Most countries do not have laboratory tests, like CBC, TBC and cardiac out measurement are rare [36]. In addition, tests must be performed in a biosafety level - 4 laboratory.

If the patient cannot maintain fluid balance because of gastrointestinal illness, IV crystalloid fluids should be administered [37]. Hypoxia is reported to occur with Ebola virus disease. Many people have survived Ebola virus disease [38]. Their convalescent serum has been administered to others who were actually affected with Ebola virus disease with anecdotal success [39]. Early vaccines like AVI - 7537 & AVI - 7288 were used for the treatment of Ebola virus and found to be less effective for about 84% of the population [40]. A non - neutralizing antibody that cross reacts with glycoprotein effective neutralization of virus [41].

PREVENTION STRATEGIES

While licensed vaccines against Ebola virus infection are still against Ebola virus infection are still not available. A number of vaccines against Ebola virus have been developed and showed good effects among animal models. This development needs a focus and a proper, adaptable, non - harmful / Hazards vaccine can be invented [42,43]. Coordinated medical services, careful handling of infected cases are the main preventive measures of ebola virus [44]. Preventive measures can be followed by distancing from the infected people, their body fluids, and the bodies of anyone who has died from the disease. Preventive strategies must also be taken to avoid contact contact with wild reservoir animals, like bats and monkeys, and their meat.

Conclusion

Conclusively, this review had highlighted an overview on the EBOLA virus and its immunopathogenesis. With no treatment strategies discovered yet, preventive measures are considered as the best method from acquiring the disease. Conventional, serological and molecular methods are available to detect and screen the viral markers with limitations. This review also emphasizes on the need for vaccine and drug discovery against EBOLA virus.

AUTHOR CONTRIBUTIONS :

S. UMAYAL

1. Execution of the work.
2. Data collection.
3. Drafting of Manuscript.

SMILINE GIRIJA . A.S

1.Concept and design of the study.

2. Validation of the data collections.

3. Revision and proofreading of the review

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